IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Palazzini *et al.*	Confirmation No.: 4468
Serial No.: 09/873,234	Art Unit: 1623
Filed: June 4, 2001	Examiner: Patrick T. Lewis
For: METHODS AND COMPOSITIONS USING SULODEXIDE FOR THE TREATMENT OF DIABETIC NEPHROPATHY	Attorney Docket No.: 9457-023

DECLARATION OF DR. ROBERT M. NIECESTRO UNDER 37 C.F.R. § 1.132

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Robert M. Niecestro, Ph.D., do hereby declare and state:

1. I am currently Vice President, Clinical & Regulatory Affairs of Keryx Biopharmaceuticals, Inc., which is the exclusive licensee of the above-identified patent application in the United States.

2. My academic background, technical experience and list of publications are set forth in my *curriculum vitae*, attached hereto as Exhibit 1.

EFFECTS OF GLYCOSAMINOGLYCANS AS A DRUG CLASS

3. Sulodexide belongs to a class of drugs known as glycosaminoglycans (GAG). Although the exact mechanisms of action for sulodexide and other GAGs in the treatment of diabetic nephropathy are unknown, Table 1 presents some of the possible potential beneficial effects of this drug class from non-clinical studies.

Table 1

Benefits of Sulodexide in the Treatment of Diabetic Nephropathy

Renal Abnormality	Effects of Glycosaminoglycans
Thickened Glomerular Basement Membrane (GBM)	Prevention and correction of the thickening GBM (Gambaro et al., Kidney Int 1992; 42:285-291; Gambaro et al., Kidney Int 1994; 46:797-806)
Diminished GBM anionic charge barrier	Prevention and correction of diminution of GBM anionic charge barrier (Gambaro et al., Kidney Int 1994; 46:797-806)
	Via direct deposition in the GBM (Ofusu, Semin Thromb & Hemost 1998; 24(2):127-138)
	Via Inducuction of heparan sulfate proteoglycan synthesis and sulfation (Nader et al., J Cell Physiol 1989; 140(2):305-310)
Dimished GBM anionic charge barrier	Via inhibition of heparanase (Xu et al., JASN 2005; 16 (Abstract Issue) Poster-Sa-PO534
Mesangial cell proliferation (early)	Suppression of pathological mesangial cell proliferation (Caenazzo et al., Nephrol Dial Transplant 1995; 10(2):175-184)
Excessive expression of mesangial matrix proteins	Suppression of TGF-β1 mediated collagen IVα1 and fibronectin transcription of collagen IVα1 and fibronectin in mesangial cells (Caenazzo et al., Nephrol Dial Transplant 1997; 12(3):443-448; Oturai et al., Diabetes 1997; 46:120A; Wang et al., Nephrol Dial Transplant 1998; 13:3052-3057)
Albuminuria induced and endothelin mediated tubulo-interstitial inflammation and fibrosis	Suppression of albuminuria induced and endothelin mediated tubulo-interstitial inflammation and fibrosis (Yokokawa et al., J Am Soc Nephrol 1994; 4:1683-1689; Reantragoon et al., Arch Biochem Biophys 1994; 314:315-322; Zoja et al., Am J Kid Dis 1995; 26:934-941)
Apoptosis	Inhibition of apoptosis in glomerular cells (Ishikawa et al., Kidney Int 1999; 56(3):954-63)
Arterial smooth muscle	Inhibition proliferation of arterial smooth muscle cells (Tiozzo et al., Arzneim-Forsch/Drug Res 1989; 39:15-20)
Thrombus	Retards thrombus progression and prevents thrombus formation and stimulates local fibrinolysis (Barbanti et al., Int J Clin Lab Res 1992; 22:179-184; Buchanan et al., Thromb Res 1994; 74(5):463-475)

BACKGROUND INFORMATION-EFFICACY OF SULODEXIDE IN DIABETIC NEPHROPATHY IN CLINICAL TRIALS

4. Prior to the Pilot Phase II study (Study KRX-101-013a) sponsored by Keryx Biopharmaceuticals, Inc., Alfa Wasserman, the sole assignee of the present application, conducted eight small clinical trials (Table 2) and a Phase II multicenter,

double-blind, randomized dose-range finding study with orally administered sulodexide in patients with diabetic nephropathy (Study No. V2F/DRF/95 or "the DiNAS study"). In these studies, unless otherwise specified, dose levels of sulodexide are expressed by the authors in either LSU or LRU (lipoprotein lipase releasing units). One mg of sulodexide = 12 ± 2 LSU.

5. In reviewing these eight clinical studies enrolling 185 patients with diabetes, comprised the initial database for sulodexide in the treatment of diabetic nephropathy, Gambaro and Van der Woude, J Am Soc Nephrol 2000; 11:359-368, noted the consistency of AER or albuminuria reduction across all studies, despite the less than desirable study design methodology used in some. They noted that the results were comparable to studies reported with low molecular weight heparin ("LMWH"), enoxaparin, and danaparoid, but differed from the absence of reduction in AER seen in a study with tinzaparin. They suggested that this may have been due to the rather low dose of LMWH given in the latter trial. Although these authors stated that treatment of diabetic nephropathy with glycosaminoglycans (GAGs) can be viewed as an experimental test of the Steno hypothesis, this group of studies, although promising, were probably too small and too short in duration to clarify whether GAG treatment in diabetic nephropathy patients is capable of curing diabetic nephropathy or just simply influencing one of its surrogate endpoints, albuminuria. The overall positive experience from this initial group of eight studies led to the design and completion of the DiNAS study by Gambaro et al., J Am Soc Nephrol 2002; 13:1615-1625 and Alfa Wasserman, the sole assignee of the present invention.

Table 2: Clinical Efficacy Studies with Sulodexide for Diabetic Nephropathy

Study Title or Reference	Study Design	Patients	Formulation	Route	Duration	Doses
Solini et al., Diab Care 1997; 20(5): 819-823	random, double-blind, placebo-controlled, crossover	12 DM2	enteric coated tablet	PO	4 months	0 or 100 mg/day
Velussi et al., Diab Nutr Metab 1996; 9:53-58	open label, random, cross over	24 DM2	gel cap	PO	6 months	2 x 25 mg b.i.d. (100 mg/day)
Poplawska et al., Diab Res Clin Pract 1997; 38:109-114	open label	14 DM1	Vessel Due F	IM	31 days	60 mg/day IM x 10 days then 25 mg PO b.i.d. x 21 days
			gel cap	PO		
Solini et al., Diab Nutr Metab 1991; 7:301-305	open label	11 DM2	gel cap	PO	2 months	100 mg/day
		5 DM2	not indicated	IM	3 weeks	60 mg/day
Dedov et al., Neprhol Dial Trans 1997; 12:2295-2300	open label, random, placebo-controlled	36 DM1	Vessel Due F	IM	3 weeks	0 or 60 mg/day (5 days/week)
Szelanowska et al., Curr Med Res Opin 1997; 13(9):539-545	open label	15 DM1	Vessel Due F	IM	3 weeks	60 mg/day
Škrha et al., Diab Res Clin Prac 1997; 38:25-31	open label	26 DM1 27 DM2	Vessel Due F	IM	3 weeks	60 mg/day
Sorrenti et al., J Int Med Res. 1997; 25(2):81-86	open label	15 DM2	not indicated	IM	4 weeks	60 mg/day

DM1 = type 1 diabetes mellitus; DM2 = type 2 diabetes mellitus

6. The objective of the DiNAS study (the multi-center, double-blind, randomized, dose range finding study) of the activity of sulodexide versus placebo in the treatment of micro- and macro-albuminuria in patients suffering from diabetes nephropathy (Study No. V2F/DRF/95) was to evaluate the safety and efficacy of three different doses of sulodexide (50, 100 or 200 mg/day) versus placebo administered for four months in type 1 diabetes mellitus ("DM1") and type 2 diabetes mellitus ("DM2") patients with diabetic nephropathy. Alfa Wassermann conducted this study from October 1996 to December 1998.

7. Two hundred and twenty-three patients with DM1 or DM2 and with urinary albumin excretion ratio ("AER") between 20 and 200 µg/min (micro-albuminuric) or with AER over 200 µg/min (macro-albuminuric) were enrolled. Sulodexide gelcaps (25 mg) or identical placebo gelcaps were administered. Patients were randomly assigned to treatment with placebo, 25 (total daily dose of 50 mg), 50 (total daily dose of 100 mg), or 100 mg (total daily dose of 200 mg) *b.i.d.* (twice a day) of sulodexide. All patients received four gelcaps of sulodexide and/or identical placebo orally *b.i.d.*, so that double blinding was strictly maintained. Assigned treatment was continued for four months, and follow up was maintained for an additional four months. The main outcome assessed was urinary AER that was measured via the mean of three consecutive timed overnight AER determinations. These determinations were made prior to treatment, at the end of the four months of treatment, and at the end of the additional four months of follow up without treatment. Inclusion criteria included stable blood pressure less than 160/90 mm Hg (either spontaneously or due to pharmacological intervention) for six months prior to enrollment and serum creatinine <150 µmol/L (150 mg/dL).

8. The percent reduction in AER at the end of the four-month treatment was significantly different from placebo, and approximately linear to dose increments. The sulodexide 50 mg/day group had a 30% AER reduction ($p = 0.0282$), the sulodexide 100 mg/day group had a 49% AER reduction ($p = 0.0001$), and the sulodexide 200 mg/day group had a 74% AER reduction ($p = 0.0001$) (Table 3). In addition, in the group treated with 200 mg/day of sulodexide, a strong residual effect on lowering of log AER was noted four months after drug administration was stopped ($p = 0.0001$) (Table 4).

9. Subanalysis of subjects on concomitant angiotensin converting enzyme (ACE) inhibitor treatment versus those not receiving ACE inhibitors showed nearly superimposable

results (Table 5). Sulodexide was also equally effective in DM1 and DM2 and in micro- and macro-albuminuric patients.

Table 3: Efficacy of Sulodexide at Completion of 4-Month Treatment with Sulodexide

Group	N	Log Adjusted Mean	Log Standard Error	AER Percent Reduction	p-value versus Placebo	
					Parametric	Non-parametric
Placebo	52	5.31	0.11	--	----	----
50 mg	51	4.95	0.12	30%	0.0282	0.0026
100 mg	50	4.63	0.12	49%	0.0001	0.0001
200 mg	53	3.98	0.11	74%	0.0001	0.0001
	206					

Table 4: Efficacy of Sulodexide at Completion of Follow-up

Group	N	Log Adjusted Mean	Log Standard Error	AER Percent Reduction	p-value versus Placebo	
					Parametric	Non-parametric
Placebo	49	5.07	0.13	--	----	----
50 mg	48	5.05	0.13	2%	0.9202	0.9660
100 mg	49	4.73	0.13	29%	0.0715	0.0179
200 mg	53	4.11	0.13	62%	0.0001	0.0001
	199					

Table 5: AER Reduction Following Treatment with Sulodexide in DM1 and DM2 Patients, With and Without ACE Therapy

Group	DM1		DM2		Micro		Macro		ACE Inhibitors			
									Yes		No	
	T4	T8	T4	T8	T4	T8	T4	T8	T4	T8	T4	T8
50 mg	16%	0%	47%**	12%	30%	0%	35%*	20%	35%*	12%	27%	-5%
100 mg	48%**	38%	52%**	18%	50%*	25%	49%**	42%*	51%**	28%	48%*	36%
200 mg	70%**	62%**	77%**	63%**	74%**	65%**	74%**	62%**	74%**	60%**	74%**	67%**

T4 = end of 4-month treatment period
T8 = end of 4-month washout (without sulodexide treatment)
* denotes p-value ≤ 0.05
** denotes p-value ≤ 0.001

10. In conclusion, four-month treatment with sulodexide gelcaps in doses of 50, 100, and 200 mg/day caused significant diminutions in log AER in DM1 and DM2 patients with micro- and macro-albuminuria. Normoalbuminuria was achieved in 42% of patients receiving a 200 mg daily dose of sulodexide, and in 14% of patients receiving placebo. Reductions in AER were equivalent in patients treated concomitantly with ACE inhibitors and those not treated with ACE inhibitors. The dose to response relationship noted was a linear one. Statistically significant residual AER lowering effects were noted in the 200 mg/day treated group four months after sulodexide was discontinued.

11. Thus, sulodexide appeared efficacious among all diabetic albuminuric patient populations, and its beneficial effects on AER reduction appear additive to those achieved with concomitant ACE inhibitor therapy. Further, at the 200 mg dose in patients with and without concomitant ACE inhibitors, sulodexide produced reductions in AER that persisted at least four months after sulodexide treatment was discontinued. This suggests that treatment with sulodexide may have induced structural (*i.e.*, anatomical) changes in renal tissues, perhaps by replenishing endothelial heparin sulfate. This phenomenon is unprecedented, as AER levels are reported to rise rapidly and precipitously upon discontinuation of ACE inhibitor therapy (Hansen et al., Kidney Int. 1995; 48(5):1559-62). Thus, the unprecedented fact that a 200 mg dose of sulodexide provided long term reductions in AER is proof that the 200 mg dose of sulodexide is highly advantageous over the 100 mg dose.

12. Based on the proposed mechanism of actions in animal studies and the linear dose- response seen in the DiNAS study with a total daily dose of 50, 100, and 200 mg, it was hypothesized that the total daily dose of 400 mg dose (200 mg bid) in the Pilot Phase II study (Study KRX-101-013a) would do the following:

1. Continue the linear dose-response shown in the DiNAS study and thus it was expected that the 400 mg dose would show a greater reduction in AER greater than 200 mg dose in the DiNAS study;

2. Since it was demonstrated in the DiNAS study that sulodexide efficacy was not affected by the use of ACE inhibitors, it was expected that based on the results from the DiNAS study that the 200 mg results in Study KRX-013a should be similar to the results from the DiNAS study with the 200 mg dose and that the

proposed 400 mg dose in Study KRX-101-013a should be at least similar to the 200 mg in the DiNAS, if not superior; and

3. It was expected that the 400 mg dose would be at least equal to or better than the 200 mg dose in Study KRX-101-013a in terms of the following:

   a. Observed Albumin to Creatinine Ratio ("ACR") level;

   b. Percentage of Patients Achieving Therapeutic Success (defined as a binary composite endpoint defined as conversion to normoalbuminuria (ACR < 20 mg/g) and a 25% reduction in ACR level relative to baseline, OR a 50% reduction in ACR level relative to baseline); and

   c. The percentage of patients achieving normoalbuminuria.

RESULTS FROM STUDY KRX-101-013A

13. Study KRX-03-013a was randomized, double-blind, placebo-controlled, multi-center, multi-dose study of sulodexide for the treatment of type 2 diabetic nephropathy patients with persistent micro-albuminuria. In this study, two doses of sulodexide (200 mg and 400 mg) were compared to placebo in patients with diabetic micro-albuminuria on maximal therapy with either an ACEi or ARB. Patients were treated with sulodexide or placebo for six months and followed for an additional two months post-treatment. Patients were randomized 1:1:1 to placebo, 200 mg and 400 mg of sulodexide, respectively. In this Phase 2 study, the primary endpoint for the study was the percentage of patients achieving "therapeutic success" at six months. A patient was documented as having "therapeutic success if they achieved one of the following outcomes at six months on the study: (1) a 50% reduction in ACR or (2) normalization of ACR with at least a 25% reduction in ACR. In this study, the normal laboratory range for albuminuria was defined as less than 20 mg of albumin to 1 g of creatinine.

14. A total of 149 patients were randomized into the study. All patients evaluable for "therapeutic success" at six months (*i.e.*, all patients with a baseline ACR and six-month ACR) were included in the Intent-to-Treat ("ITT") analysis, for a total of 136 patients in the ITT population. All patients in the ITT population that at baseline were within the target eligibility range of micro-albuminuria as defined in the protocol (ACR 20 mg/G to 200

mg/G) were included in the Per-Protocol ("PP") analysis for a total population of 117 patients in the PP population. All of the primary and secondary analyses shown were pre-specified. For the primary endpoint analysis, statistical nominal p values have been provided for informational purposes only since this Phase 2 study, as a pilot study, had less than a 20% power to show statistically significant results for these endpoints.

Table 6: Primary Endpoint Analysis (Therapeutic Success at Six Months) (200 and 400 mg of Sulodexide vs. Placebo)

Group	Number of Patient (Placebo/Active)	Placebo	Active (200 and 400 mg KRX-101)	p-value (Fisher's Exact Test (Two-Sided)
Intent-to-Treat	42/94	14%	26%	p = 0.180
Per Protocol	36/81	11%	25%	p = 0.136

Table 7: Primary Endpoint Analysis (Therapeutic Success at Six Months) (200 mg of Sulodexide vs. Placebo)

Group	Number of Patient (Placebo/Active)	Placebo	Active (200 mg KRX-101)	p-value (Fisher's Exact Test (Two-Sided)
Intent-to-Treat	42/44	14%	32%	p = 0.074
Per Protocol	36/36	11%	33%	p = 0.045

Table 8: Primary Endpoint Analysis (Therapeutic Success at Six Months) (400 mg of Sulodexide vs. Placebo)

Group	Number of Patient (Placebo/Active)	Placebo	Active (200 mg KRX-101)	p-value (Fisher's Exact Test (Two-Sided)
Intent-to-Treat	42/50	14%	18%	NS
Per Protocol	36/45	11%	20%	NS

NS = Non Significance

Table 9: Secondary Endpoint Analysis at Six Months (ITT)

Parameter	Placebo	200 mg	400 mg	Active (200 mg and 400 mg combined)
Number of	42	44	50	94

Subjects				
> 50% reduction in ACR	12%	27%	18%	22%
Normalization of ACR	9%	23%	10%	17%

Table 10: Average Changes in ACR over Time (ITT)

	200 mg vs. Baseline	400 mg vs. Baseline	Placebo vs. Baseline
Two Months	-21.00%	3.4%	-4.0%
Four Months	-18.28%	3.24%	7.5%
Six Months	-15.46%	5.59%	12.57%
Eight Months (Two Months Off Therapy)	-10.48%	12.59%	18.5%

15. The final efficacy results with the 400 mg dose of sulodexide from the Pilot Phase II study (Study KRX-101-013a) were totally unexpected. It was hypothesized prior to the initiation of Study KRX-101-013a that the 400 mg dose of sulodexide would be at least equal to or superior to the 200 mg dose. The finding in Study KRX-101-013a that the 400 mg was less efficacious, no further dose-response was documented, no plateau in the dose-response was observed with a 400 mg dose, and a decrease in the efficacy of the 400 mg as compared to the 200 mg was unexpected and clearly demonstrates that a dose of approximately 200 mg of sulodexide represents the best dose for the treatment of diabetic nephropathy. Increasing the dose of sulodexide from 200 mg to 400 mg with no increase in the efficacy of sulodexide was totally unexpected. The following findings regarding the efficacy of the 400 mg dose of sulodexide were totally unexpected:

1. The 400 mg dose was less efficacious in normalizing micro-albuminuria and was therefore less effective than 200 mg.

2. The 400 mg dose was less efficacious in reducing ACR by > 50% as compared to 200 mg.

3. The average change in ACR versus baseline over time was different between the 200 and 400 mg dose of sulodexide. Based on a review of the data, the 400 mg

dose of sulodexide never reduced ACR; while the 200 mg dose of sulodexide clearly reduced ACR. This finding was unexpected.

4. In the eight small Pilot II studies, the DiNAS study, and with the 200 mg dose of sulodexide in KRX-101-013a study, the effects of sulodexide on lowering either ACR or AER were seen approximately two to four months off therapy, while the 400 mg dose of sulodexide in Study KRX-101-013 did not show a similar prolonged effect. This finding was never anticipated and clearly shows that the 400 mg dose of sulodexide is working fundamentally different than the 200 mg in terms of restoring the anionic charge of the glomerular basement membrane.

16. In view of the unexpected results of the 200 mg dose of sulodexide providing long term reduction in AER as compared to the 100 mg dose and the fact that the 400 mg dose of sulodexide was less efficacious that the 200 mg dose, it is my opinion that a dose of about 200 mg per day of sulodexide for the treatment of diabetic nephropathy is a peak or optimum dosage for sulodexide in which dosages higher and lower have been shown to have less efficacy. The fact that sulodexide has a peak dosage is wholly unexpected in view of the results of the clinical trials in which 50 mg, 100 mg or 200 mg had been given as the dose response in those studies was linear, *i.e.*, the higher the dose, the greater the efficacy.

17. I declare further that all statements made in this Declaration of my own knowledge are true, and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and that like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 19 of the United States code and that such willful false statements may jeopardize the validity of this application and any patent issuing thereon.

Dated: 26 Sept 06

Robert M. Nicecstro, Ph.D.

ROBERT M. NIECESTRO, Ph.D.
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Approximately 20 years experience in managing and directing pharmaceutical research and development, clinical development, regulatory affairs, and project management.
Experience includes the following:

- Leading international development teams to advance new molecular entities from discovery to registration in major world markets;
- Providing the strategic and regulatory vision and tactical focus for assigned projects from filing INDs to negotiating final package labels
- Establishing the mission goals for assigned projects as defined by the proposed therapeutic use, proposed market claims, and regulatory guidelines;
- Determining both the external and internal resources required and managing the execution of the development plans consistent with the corporate goals, approved budgets, milestones, and regulatory constraints;
- Out-sourcing effectively with Clinical Research Organization;
- Strategies for In-Licensing and Out-Licensing new drugs; and
- Effectively interacting with worldwide regulatory agencies.

Therapeutic areas of development include the following: Central Nervous System, Stroke, and Alzheimer Disease; Cardiovascular and Anti-thrombotics, Reproductive Medicine and In-Vitro Fertilization; Endocrinology (Diabetes and Hyperlipidemia); Oncology; Gastrointestinal; Dermatology; Nephrology; and Urology.

EMPLOYMENT HISTORY:

Keryx Biopharmaceuticals, Inc.

02/02/03 to Present Vice-President Clinical and Regulatory Affairs

Currently managing the following trials:

1. The effects of sulodexide in early diabetic nephropathy-Phase III study in approximately 1000 patients-Special Protocol Assessment (SPA) with FDA-first surrogate marker study using proteinuria granted under SPA by FDA
2. The effects of sulodexide in overt diabetic nephropathy-Phase IIIb/IV study in approximately 2200 patients-Special Protocol Assessment with FDA
3. The effect of sulodexide on prolonging the QTc interval-Phase I study in approximately 48 healthy volunteers
4. Two-year carcinogenicity study in rats and mice with sulodexide-Special Protocol Assessment with FDA

5. Non-clinical and clinical development of a NGF enhancer for the treatment of Alzheimer's disease and Huntington's disease.
6. The non-clinical and clinical development of ferric citrate in lowering serum phosphorus levels in patients with chronic kidney disease-Phase II/III in approximately 300 to 600 subjects in the US and Israel

Memberships:

Regulatory Affairs Professional Society
Association of Clinical Research
International Society of Regulatory Toxicology and Pharmacology
Genetic Toxicology Society
Association of Human Pharmacology
Safety Pharmacology Society
Academy of Pharmaceutical Society
Royal Pharmaceutical Society of Great Britain
The Organisation for Professionals in Regulatory Affairs (Europe)
Licensing Executive Society International
National Catholic Bioethic Center
American Society of Bioethics and Humanities
International Association of Bioethics

I am the registered regulatory representative for Keryx with the following worldwide regulatory agencies:

United States: Food and Drug Administration; Australia: Department of Health and Ageing Therapeutic Goods Administration; Austria: Federal Ministry for Health and Women; Belgium: Directorate general for the protection of Public health: Medicines; Canada: Health Canada; Denmark: Danish Medicines Agency; Finland: National Agency for Medicines; France: Ministry of Health; Germany: Federal Institute of Drugs and Medical Devices; Hong Kong: Department of Health; Hungary: National Institute of Pharmacy; Ireland: Irish Medicines Board; Israel: Israeli Health Ministry Pharmaceutical Administration; Italy: National Monitoring Centre for Clinical Trials - Ministry of Health; Netherlands: The Central Committee on Research Involving Human Subjects (CCMO); New Zealand: Health and Disability Ethics Committees; Poland: Ministry of Health; Portugal: National Pharmacy and Medicines Institute; Spain: Spanish Agency of Medicines; Sweden: Medical Products Agency; Switzerland: Swissmedic; United Kingdom: Medicines and Healthcare Products Regulatory Agency.

Andrx Labs. Hackensack, New Jersey

01/02/03 to 02/01/04	Vice President, Pre-Clinical and Clinical Development and Regulatory Strategy
02/14/01 to 12/31/02	Executive Director, Nonclinical and Clinical Research

Reporting to the Executive Vice-President Research and Development, I was responsible for the following departments: Preclinical, Clinical Pharmacokinetics, Clinical Development, Project Management, and NDA and MAA filings. The following drugs were developed and filed under my leadership:

- Altocor (lovastatin extended-release)-NDA and MAA
- Fortamet (metformin extended-release)-NDA and MAA
- Valproate type compound-NDA only
- Metformin-pioglitazone combination-IND, Pre-Clinical and Clinical Development
- Antacid-Proton Pump Inhibitor Combination-Formulation Development, IND, Pre-Clinical and Clinical Development (OTC)
- Claritin (Rx to OTC switch)

Eisai Inc. Teaneck, New Jersey

10/01/99 to 10/05/00	Senior Director, Research and Development Gastrointestinal, Oncology, and Stroke Member: Global R & D Committee (Since 8/98) Member: Global Clinical Committee (Since 8/98)
08/20/97 to 10/01/99	Director, Research and Development Planning

Reporting to the Vice President of Clinical Research and Development, I was responsible for the following areas:

Gastrointestinal (Aciphex/Pariet as the International Project Team Leader)

- Eradication of Helicobacter pylori
- Relief of Symptomatic GERD
- Pediatric Program
- Rx to OTC Switch
- Post-NDA Commitment Program
- Technical assessment of potential in-license candidates

Stroke:

- The overall development plans for CAND, a neuron-specific calcium channel blocker.
- Technical assessment of potential in-license candidates in the Stroke area

Director, Research and Development Planning
Reporting to the Vice President of Research and Development, I was responsible for for the following: assisting in the development of the regulatory strategy, project management, resource planning, and budgets for all development programs within Eisai Inc. These include the Neurology (Aricept™, CAND, and SAAS), Anti-Infectives/Sepsis (E-5564 and CZZZ), GI (Aciphex™), Oncology, (BOLD, GOAL, and LIFE) and Internal Medicine programs (CERT, RAIL, SQAL).

Appointed to the Global and Development Committee and Global Clinical Committee on August 20, 1998, by President Naito. Responsibilities include developing regulatory and program/project management strategies for all compounds globally.

Developed and implemented business procedures for the management of Eisai's drug portfolio globally with the Strategic Decision Group of Palo Alto, California. (Now known as Navigant)

Assigned the responsibility to organize the International Project Team for rabeprazole to submit a NDA to the FDA by March 31, 1998, (approximately six months after joining Eisai Inc.) In addition, I assisted the International Project Team in completing four outstanding clinical programs leading to the approval of the MAA by the MCA in the United Kingdom/European Union.

Organon Inc./Akzo Nobel Pharma Division West Orange, New Jersey

03/31/97 to 08/17/97	Director, Clinical Trials Operations
01/15/96 to 03/31/97	Director, Clinical NDA Planning and Drug Development
01/15/96 to 03/31/97	Director, Clinical Projects-Cardiovascular & Thrombosis
08/01/94 to 11/01/96	Special Assignment to the Board of Directors for Organon
05/16/94 to 01/15/96	Director, Clinical Projects-Parenteral Group
09/14/92 to 05/16/94	Clinical Project Director & Project Leader-Cardiovascular Clinical Project Director-Anesthesiology (till 10/30/93)
09/30/91 to 09/14/92	Clinical Project Director – Anesthesiology
11/10/90 to 09/30/91	Assistant Clinical Project Director

Director, Clinical Trials Operations

Assigned the responsibility to direct four departments (Drug Safety, Monitoring, Clinical Documentation, and Data Management) with approximately 70 employees.

Director, Clinical NDA Planning and Drug Development

This position involved managing a multi-disciplinary, multi-departmental International NDA Project team utilizing a functional-matrix model of regulatory-project management. Assigned the responsibility to plan and direct the submission of three NDAs and one sNDA in 1996 to 1998 in two distinct therapeutic areas (reproductive medicine and neurology). The sNDA was for Orgaran™ (Org 10172) for the treatment of acute ischemic stroke. The sNDA was to be filed based on the results from on highly powered "adequate and well-controlled" clinical trial. The sNDA for Orgaran™ was not filed due to the failure of meeting the primary objective of the study. The NDA for one drug in the reproductive area was submitted in March 1997 and approved in April 1998 (Merulax™). The other two NDAs were not submitted to the FDA.

Special Assignment to the Board of Directors for Organon

Assigned to a special committee reporting to the Board of Management for Organon to re-engineer the clinical development process and to define the global integration strategies for research and development. Major achievements of the team are as follows:

- For short-term parenterals the research and development process from drug discovery to registration in both Europe and the US now approximately three to five years.
- For long-term parenterals, orals, and implants, the research and development process from drug discovery to registration in both Europe and the US is approximately four to six years.
- A fully integrated global clinical and safety database, including serious adverse events.
- A fully integrated global international project teams with fixed standard operating procedures, integrated databases, and case report forms.

Director, Clinical Projects – Cardiovascular & Thrombosis/Pro-Fertility

Responsibilities included managing the clinical development programs globally or in the U.S. for the following therapeutic areas: Pro-fertility [Humegon, recombinant FSH (Org 32489), recombinant LH, Ganirelix (U.S. development); Anesthesiology [Intravenous Anesthetic (U.S. development); and Cardiovascular [Orgaran™ (Org 10172) and Org 31540/SR 90107A (global development)].

Under my supervision two NDAs [Orgaran™ (Org 10172) for the prophylaxis of DVT following hip replacement surgery and Follistim™ (Org 32489) for in-vitro fertilization] were filed and three NDAs (Humegon™, Orgaran™, Follistim™) were approved. Assigned the Pro-fertility area in May 1994, and was able to re-analyze the data and interact with the FDA to obtain the approval of Humegon™ (the first pro-fertility product in the U.S. for Organon) by the end of September 1994. Under my supervision four INDs were filed (Org 32489, Ganirelix, Org 31540/SR 90107A, and Orgaran™ for the treatment of non-hemorrhagic ischemic stroke). Follistim™ was approved by the FDA based on data from Europe and prior to the submission of an IND.

Global responsibilities for managing both the clinical development programs for Pentasaccharide for Organon for the prophylaxis of DVT and Orgaran™ for the treatment of non-hemorrhagic ischemic stroke. Lead the clinical data development team in establishing an integrated global database system for the Pentasaccharide program for four operating divisions (Organon-U.S., Organon-Europe, Sanofi-Europe, and Sanofi-Winthrop-U.S.) for Org 31540/SR90107A. Directed the TOAST Program (use of Org 10172 in the treatment of acute or progressing non-hemorrhagic ischemic stroke). A study co-sponsored with NIH-NINDS, involving over 45 sites and 1300 patients.

Regulatory, scientific and technical liaison member of the Project Introductory team for the Marketing Department for the following drugs: Humegon™, Follistim™, and Orgaran™.

Coordinate the clinical sections for the Interactive NDA (NDA 20-214) for Zemuron™ (rocuronium bromide); injection with the Pilot Division. NDA submitted by CANDA: June 29, 1993, NDA Day (Advisory Sub-Committee Meeting); October 7, 1993; NDA Approval Letter from FDA: March 17,1994.

Submitted two NDAs using population pharmacokinetics [NONMEM (Zemuron™) and P-Pharm (Orgaran™)].

Provided Executive Management monthly updates of tasks and milestones and present status updates at all quarterly board meetings.

Served as the Clinical Project Director for two pharmacokinetic studies (Pharmacokinetics, Bioavailability, and Dose Proportionality for Org 10172 and a four-way cross over bioequivalency study using population Pharmacokinetics).

Hollister Incorporated Libertyville, Illinois

12/88 to 11/90	Senior Clinical Programs Coordinator
10/86 to 12/88	Clinical Research Coordinator

Corporate Project Leader, Co-Developer, and Clinical Coordinator for the first FDA-approved non-pharmacological therapeutic modality for managing psoriasis. Presented proposed primary defect in psoriasis at the American Federation of Clinical Research and the American Academy of Dermatology in 1989 based on the work-related to the development of Restore™ Dressing for Psoriasis.

Clinical Coordinator of the Hollister Infusion Pump for oncology or antibiotic infusion. Coordinated the drug sterility program for the drug reservoir. Managed the Phase I/II drug delivery and pharmacokinetic studies in the Oncology area.

Clinical Coordinator for the following non-clinical and clinical programs:

- Genetically derived growth factors (EGF and bet-TGF) in wound healing
- Collagen and collagen implants in wound care and dermatology
- Calcium channel blocker for bladder instability

Managed clinical studies on the following products:

- Restore™ Wound Care Dressing
- HOT/ICE™ system for pain and inflammation management
- Orthopedic external braces
- Peptide fragments as growth factors

EDUCATION

Undergraduate
1975 to 1979, Bachelor of Science, University of Illinois at Chicago – Chicago, Illinois (Biological Science)

Graduate
1980, Doctoral Summer Course Work, Illinois Institute of Technology – Chicago, Illinois (Biochemistry)
1982 – 1985, Doctor of Philosophy, Pharmacology/Biochemistry Rush University – Chicago, Illinois /Somer
Biochemistry Thesis: Mathematical Model for Determining Potential Carcinogenic Compounds Based on a Modified Plasmid pBR322 [Research grant provided and work done on behalf of Imperial Chemical Industry (ICI) and BW BIOTEC through the Co-Operative Academic Science and Engineering Program (CASE)]

Post-Graduate
1985-1986, Post Graduate Work, University of Illinois at Chicago – Chicago, Illinois, (Microbiology) with Associate Dean/Professor M.L. Goldman, Ph.D.

I organized a specific program to identify microorganisms that degraded oil-related products. Genetically engineered *Pseudomonas* with plasmid vectors to degrade oil-related products, and enhanced natural mixed cultures of microorganisms to degrade metal working fluids before discharge into the environment.

Publications/Abstracts/Posters

Antidiabetes

Knipnes M , Niecestro RM. Comparison of extended-release metformin versus immediate-release metformin. The 13th Annual Meeting and Clinical Congress of AACE, April 28, 2004 to May 2, 2004, Boston, MA. Abstract #100 Endocrine Practice 2004 March/April; 10 (suppl 1): 35.

Niecestro RM, Knipnes M. Comparing the efficacy and tolerability of Metformin XT given daily to immediate-release metformin given twice daily in patients with type 2 diabetes. The 13th Annual Meeting and Clinical Congress of AACE, April 28, 2004 to May 2, 2004, Boston, MA. Abstract #99 Endocrine Practice 2004 March/April; 10 (suppl 1): 34-35.

Cullen E, Liao J, Lukacsko P, Niecestro RM Friedhoff LT. Pharmacokinetics and dose-proportionality of extended-release metformin following administration of 1000, 1500, 2000, and 2500 mg in healthy volunteers. Biopharmaceuticals and Drug Disposition 2004 September 25 (6) 261-263. (Published Online: 7 Jun 2004).

Niecestro RM, Isaacsohn J. Sterman A, Friedhoff LT, Brett V, Cullen EI. Comparison of lipid control with 2000 and 2500 mg of Metformin XT vs. immediate-release metformin in patients with type 2 diabetes. Abstract published at 63rd Scientific Sessions Meeting of the American Diabetic Association (ADA); June 13-17, 2003; New Orleans, LA Abstract #2142. Diabetes 2003 June; 52 (suppl 1): A494.

Niecestro RM, Lukacsko P, Walters EJ, Isaacsohn J, Friedhoff LT, Sterman A, Cullen EI. Safety and efficacy of 2000 and 2500 mg of Metformin XT to. immediate-release metformin in patients with type 2 diabetes. Abstract published at 63rd Scientific Sessions Meeting of the American Diabetic Association (ADA); June 13-17, 2003; New Orleans, LA Abstract #1907. Diabetes 2003 June; 52 (suppl 1): A440.

Niecestro RM, Sterman A, Friedhoff LT, Isaacsohn J, Brett V, Cullen EI. Safety of Metformin XT compared to immediate-release metformin. Abstract published at 63rd Scientific Sessions Meeting of the American Diabetic Association (ADA); June 13-17, 2003; New Orleans, LA Abstract #1908. Diabetes 2003 June; 52 (suppl 1): A440.

Niecestro RM, Lukacsko P, Lamson MJ, Walters EJ, Friedhoff LT. Multiple-dose pharmacokinetics of extended-release metformin. 31st Annual Meeting of the American College of Clinical Pharmacology, September 21-23, 2002, San Francisco, California, Abstract #51. J Clin Pharm 2002; 42:1062.

Niecestro RM, Lukacsko P, Sterman AB, Lamson MJ, Walters EJ, Friedhoff LT. Pharmacokinetics of extended-release metformin vs. immediate-release metformin in Type 2 diabetic patients. Annual Meeting of the American College of Clinical Pharmacology, September 21 to 23, 2002, San Francisco, California, Abstract # 54t. J Clin Pharm 2002; 42:1062.

Niecestro RM, Lukacsko P, Lamson M, Walters EJ, Friedhoff LT. Pharmacokinetics of extended-release metformin versus immediate-release metformin in healthy subjects. Annual Meeting of the American College of Clinical Pharmacology, September 21 to 23, 2002, San Francisco, California, Abstract # 53 J Clin Pharm 2002; 42:1062.

Cullen E, Niecestro RM, Lamsom M, Walters E, Murphy M, Friedhoff LT. Dose-exposure relationship of Metformin XT. Abstract Number 517-P American Diabetes Association's 62nd Scientific Sessions, June 14-18, 2002, San Francisco, California..

Niecestro RM, Lukacsko P, Walters E, Friedhoff LT, Isaacsohn J. Effect of food on the pharmacokinetics of Metformin XT. Abstract Number 531. Poster presented at the American Diabetes Association's 62nd Scientific Sessions, June 14-18, 2002, San Francisco, California. Diabetes 2002 June; 51 (suppl 2): A131.

Lamsom M, Niecestro RM, Lukacsko P, Sterman A, Howard C, Walters E. Freidhoff LT, Isaacsohn J. Pharmacokinetics of Metformin XT versus immediate-release metformin. Abstract Number 528. Poster presented at the American Diabetes Association's 62nd Scientific Sessions, June 14-18, 2002, San Francisco, California. Diabetes 2002 June; 51 (suppl 2): A131.

Niecestro RM, Lukackso P, Walters E, Sterman A, Friedhoff LT, Isaacsohn J. Safety and efficacy of Metformin XT to immediate-release metformin in patients with Type 2 diabetes. Abstract Number 532. Poster presented at the American Diabetes Association's 62nd Scientific Sessions, June 14-18, 2002, San Francisco, California. Diabetes 2002 June; 51 (suppl 2): A131-A132.

Niecestro RM, Friedhoff LT, Cullen EI, Sterman AB, Lukacsko P, Walters E, Howard C. Effects of controlled-release metformin on the blood lipids of Type II diabetic patients [Oral Presentation]. 6th International Symposium on Global Coronary Heart Disease and Stroke: Assessment, Prevention, and Treatment. Florence (Italy), June 12-15, 2002, Abstract Book Page 23.

Hypercholesteremia

Lukacsko P, Walters EJ, Cullen EI, Niecestro R, Friedhoff LT. Efficacy of once-daily extended-release lovastatin as compared to immediate-release lovastatin in patients with hypercholesterolemia. Current Medical Research and Opionions. 2004;20:19-24.

Brett V, Niecestro RN, Messeroff J, Dailey J, Sterman A. Comparison of the cost-effectiveness of statins using a simple pharmacoeconomic model based on changes in lipid parameters. Poster presented at the 15th Annual Meeting of the Academy of Managed Care Pharmacy (AMCP); April 9 to 12, 2003; Minneapolis, Minnesota. Abstract published in JMCP 2003 Mar/Apr; 9(2): 194-5.

Crouse JR, Brett V, Niecestro RM, Lukacsko P, Penkrat V, Friedhoff LT. The percentage of patients meeting NCEP ATP III LDL-C goal in a controlled clinical trial with extended-release lovastatin. Poster presented at the Spring Practice and Research Forum of the American College of Clinical Pharmacy (ACCP); April 27 to 30, 2003; Palm Springs, California. Abstract # 18. Pharmacotherapy 2003 Mar; 23 (3): 393.

Rich SJ, Niecestro R, Brett V, Dailey J, Friedhoff, Messeroff J, Sterman A. Comparison cost of statin therapy. Poster and Abstract Accepted for Presentation at the American Society of Health-System Pharmacists. 37th Midyear Clinical Meeting. December 8 to 12, 2002.

Niecestro RM, Brett V, Friedhoff L. Therapeutic algorithm for initiation of oral therapy with a statin. . Poster and Abstract Accepted for Presentation at the American Society of Health-System Pharmacists. 37th Midyear Clinical Meeting. December 8 to 12, 2002.

Davidson M, Isaacsohn J, Lamsom M, Lukacsko P, Phillips G, Walters E, Ortiz M, Niecestro R, Freidhoff L. A multiple-dose tolerability, pharmacokinetic and pharmacodynamic study in hypercholesterolemic patients treated with extended-release lovastatin 60 mg and 120 mg per day. Am J Cardiovascular Drugs. Submitted and accepted.

Niecestro RM, et al. Therapeutic algorithm for initiation of oral therapy with a statin. Poster presented at the 37th Annual Midyear Clinical Meeting of the ASHP; December 8 to 12, 2002; Altanta, Georgia. [ASHP Midyear Clinical Meeting Abstract on Disc, 2002 37 (Dec); Abstract # p-104E].

Niecestro RM, et al. Comparison of the lipid-modifying effects and cost of extended-release lovastatin versus Therapeutic algorithm for initiation of oral therapy with a statin. Poster presented at the 37th Annual Midyear Clinical Meeting of the ASHP; December 8 to 12, 2002; Altanta, Georgia. [ASHP Midyear Clinical Meeting Abstract on Disc, 2002 37 (Dec); Abstract # p-104E].

Lamsom M, Lukacsko P, Niecestro R. Friedhoff L. Effects of food on the pharmacokinetics of lovastatin extended-release. Biopharmaceutics and Drug Disposition. Submitted and accepted. Annual Meeting of the American College of Clinical Pharmacology, September 21 to 23, 2002, San Francisco, California, Abstract Number # 52. J Clin Pharm 2002; 42:1062.

Sterman AB, Freidhoff LT, Niecestro RM, Lamson, MJ, Cullen EI. Pharmacokinetic variability of an extended-release formulation. Annual Meeting of the American College of Clinical Pharmacology, September 21 to 23, 2002, San Francisco, California, Abstract Number # 55. J Clin Pharm 2002; 42:1063.

Lamson M, Niecestro R, Walters E, Lukacsko P, Friedhoff L. Effects of food on the absorption of lovastatin following administration from an extended-release dosage form. Annual Meeting of the American College of Clinical Pharmacology, September 21 to 23, 2002, San Francisco, California, Abstract Number #56. J Clin Pharm 2002; 42:1062.

Niecestro R, Lukacsko P, Lamson MJ, Friedhoff LT. Pharmacokinetics and pharmacodynamics of extended-release lovastatin. Annual Meeting of the American College of Clinical Pharmacology, September 21 to 23, 2002, San Francisco, California, Abstract Number # 52. J Clin Pharm 2002; 42:1062.

Sun JX, Niecestro R, Phillips G, Shen J, Lukacsko P, Friedhoff L. Comparative pharmacokinetics of lovastatin extended-release tablets and lovastatin immediate-release tablets in humans. J Clin Pharmacol. 2002;42:1-7

Lamson M, Phillips G, Shen J, Lukacsko P, Friedhoff L, Niecestro RM. Pharmacokinetics of lovastatin extended-release dosage form (Lovastatin XL) in healthy volunteers. Biopharm and Drug Disposition. 2002;23:143-149.

Crouse JR, Lukacsko P, Niecestro R and the Lovastatin Extended-Release Study Group. Dose-response safety, and efficacy of an extended-release formulation of lovastatin in adults with hypercholesterolemia. Am J Cardiol. 2002;89:226-229.

Lukacsko P, Niecestro R, Sterman, Friedhoff LT. Multicenter, randomized, double-blind, placebo-controlled, parallel-group, dose-response study of an extended-release form of lovastatin in adult patients with hypercholesterolemia. Poster presented at 36th ASHP Midyear Clinical Meeting, December 2-6, 2001, New Orleans, LA. [Abstract-on-Disc, 2001; 36 (Dec); Abstract #P-431E].

Lukacsko P, Niecestro R, Sterman, Friedhoff LT. Multi-dose pharmacokinetic, pharmacodynamic and safety study of a novel extended-release form of lovastatin relative immediate-release lovastatin Poster presented at 36th ASHP Midyear Clinical Meeting, December 2-6, 2001, New Orleans, LA. [Abstract-on-Disc, 2001; 36 (Dec); Abstract #P-455E].

Lukacsko P, Sterman A, Walters E, Friedhoff LT. Niecestro R. High-dose, extended-release lovastatin enhances efficacy, Am Soc Health System Pharmacists. 36th ASHP Midyear Clinical Meeting and Exhibits, December 2-6, 2001, New Orleans, LA. [Abstract-on-Disc 2001; 36 (Dec); Abstract] #P-431E].] #p-424R].

Davidson MH, Lukacsko P, Sun JX, Phillips G, Walters E, Sterman A, Niecestro R, Friedhoff L. A multiple-dose safety, pharmacokinetic and pharmacodynamic study comparing an extended-release formulation of lovastatin with the immediate-release lovastatin formulation. Clin Therapeutics. 2002;24:112-125.

Alzheimer's Disease and Central Nervous System

Niecestro RM, Walters EJ, Cullen EI, Lukacsko P, Friedhoff LT, Sterman AB. The pharmacokinetics, pharmacodynamics, and tolerance of extended-release lovastatin in Alzheimer's disease. Annual Meeting of the American College of Clinical Pharmacology, September 21 to 23, 2002, San Francisco, California, Abstract #50. J Clin Pharm 2002; 42:1062.

Nangia A, Cullen E, Niecestro R, Friedhoff L. Pharmacokinetics of delayed-release valproate in healthy human subjects. J. Clin. Pharmacol. 2003; 43: 1032, Abstract 77.

Nangia A, Cullen E, Niecestro R, Friedhoff L. Effect of food on the pharmacokinetics of delayed-release valproate in healthy human subjects. J. Clin. Pharmacol. 2003; 43: 1032, Abstract 78.

Gastrointestinal

Presentation and Paper at the Advisory Committee Meeting in June 2002 for OTC Omeprazole Magnesium Discussing Antacid Interactions, Food Interactions, Time of Dosing of Prilosec in Relationship to Food, Efficacy and Safety of Prilosec in Relationship to Food, Lack of Patient Labeling with Proton Pump Inhibitors in Relationship to Food.

Patent Pending. Antacid-Proton Pump Inhibitor Combination. Application December 2001-Andrx Laboratories

Patent Pending. Novel Uses of Pyridine Derivatives. Application July 2000-Eisai Research Laboratories.

Lanza F, Bardhan KD, Perdomo C, Niecestro R, Barth J. Review: Efficacy of rabeprazole once-daily for acid-related disorders. Digestive Disease and Sciences 2001 March;(46):587-596.

Caos A, Moskovitz M, Dayal Y, Perdomo C, Niecestro R, Barth J: Rabeprazole for the prevention of erosive or ulcerative gastroesophageal reflux disease. Rabeprazole Study Group. Am J Gastroenterol 2000 Nov;95(11):3081-8.

Johnson D, Riff R, Perdomo C, Jaskir J, Niecestro R, Hahne W: Rabeprazole: Safety profile of a new proton pump inhibitor. Poster Digestive Disease Week. May 16-19, 1999, Orlando, Florida and Gastroenterology. 1999;116:A301.

Breiter J, Birbara C, Niecestro R, Perdomo C, Hahne W: Rabeprazole prevents recurrence of pathology and symptoms in patients with healed erosive or ulcerative gastroesophageal reflux disease. Poster. Digestive Disease Week. May 16-19, 1999, Orlando, Florida and Gastroenterology. 1999;116:A128.

Caos A, Moskovitz M, Perdomo C, Niecestro R, Hahne W: Rabeprazole for the prevention of pathologic and symptomatic relapse of erosive or ulcerative gastroesophageal reflux disease. Poster. Digestive Disease Week. May 16-19, 1999, Orlando, Florida Gastroenterology. 1999;116:A132.

Gitlin N, Bardhan KD, Perdomo C, Niecestro R: Rabeprazole is consistently effective for the treatment of acid-related diseases based on worldwide studies. Poster. Digestive Disease Week. May 16-19, 1999, Orlando, Florida. Gastroenterology. 1999 116:A266.

Gitlin N, Bardhan KD, Perdomo C, Niecestro R: Efficacy of rabeprazole 20 mg once daily for acid-related disorder. Poster. Digestive Disease Week. May 16-19, 1999, Orlando, Florida.

Cardiovascular/Stroke/Antithrombotics

Niecestro R: Designing future clinical trials to evaluate potential new molecular entities for the treatment of acute ischemic stroke. Invited Presentation. Japanese Heart Association. November 11, 1998. Tsuka, Japan.

TOAST Investigators: Low molecular weight heparinoid, Org 10172 (danaparoid) and outcome after acute ischemic stroke. JAMA. 1998;279:1265-1272.

Niecestro R: The Trial of Org 10172 for Acute Stroke Treatment (TOAST) and its implications for clinical and regulatory aspects of clinical trial design. 6th Annual Conference on Ischemic Stroke. November 6-7, 1997. Washington, D.C.

Miller L, Niecestro R, Magnani H: Successful cardiopulmonary bypass surgery with Orgaran in patients with heparin-induced thrombocytopenia. Thromb Haemost. 1997;78:446.

Miller LD, Niecestro RM, Magnani H: Successful cardiopulmonary bypass surgery with Orgaran in patients with heparin-induced thrombocytopenia. Congress of the International Society on Thrombosis and Haemostatis. Poster. June 10, 1997, Florence, Italy.

Incontinence

Wheeler J, Walter JS, Niecestro RM, Scalzo AJ: Behavior therapy for managing urinary incontinence. J Enterostom Ther. Mar-Apr1992;19(2):56-65.

Niecestro RM, Wheeler J, Nanninga J, Einhorn C, Goggin C. Use of StressCath for diagnosing incontinence. Urology Mar 1992;39(3):266-269.

Wheeler J, Niecestro R. Walter J. Comparison of a single-channel cystomer to a multi-channel cystomer. Int J Urogyn. 1991;2:90-93.

Wheeler J, Niecestro R. Urinary incontinence: managing the problem. J Enterostom Ther. Jul-Aug 1990;17(4):174-179.

Wheeler JS, Niecestro RM, Goggin CJ. Urinary incontinence: diagnosing the problem. J Enterostom Ther. Nov-Dec 1998;15(6):240-246.

Wheeler JS, Nanninga J, Einhorn C, Goggins C, Niecestro R: Evaluation of the StressCath female diagnostic catheter in detecting bladder neck descension. Poster. Annual Meeting, American Urology Association Allied. June 3, 1998. Boston, Massachusetts.

Dermatology

Rosseau P, Niecestro R; Comparison of the physicochemical properties of various hydrocolloid dressings. Wounds. 1991;3:43-48.

Niecestro R. Rosseau P. Comparison of the physicochemical properties of hydrocolloid dressing and their effects on the immune system. 3rd Annual Meeting. The Symposium on Advanced Wound Care. March 1990. Orlando, Florida

Wise RD, Niecestro RM: Comparison of Restore Dressing for Psoriasis to various topical corticosteroids in managing psoriasis. Poster P-66. 48th Annual Meeting, American Academy of Dermatology. December 2-7,1989. San Francisco, California.

Niecestro RM, Wise RD: Use of occlusion for managing psoriasis. American Federation of Clinical Research/Society of Investigative Dermatology. Invited Presentation. 1989. Chicago, Illinois.

Wise R, Niecestro R. Comparison of a hydrocolloid dressing to topical steroid in managing psoriasis. Clin Research. 1989;895.

Wise R, Niecestro RM: Comparison of a hydrocolloid dressing to topical steroids in managing psoriasis. Invited Abstract and Presentation. 4th International Symposium on Treatment of Psoriasis and Psoriasis-Arthritis. March 1989. Jerusalem, Israel.

Wise R, Jarmoszuk I, Finn S, Zeitz H, Niecestro R: Comparison of a hydrocolloid dressing to topical corticosteroids in treating psoriasis (preliminary results). Abstract and Poster. American Academy of Dermatology. June 17, 1988. New York City, New York.

Pending (Future)-Publications/Abstracts/Presentation:

Hyperphosphatemia

Niecestro RM, et al. "A Phase II, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study of Ferric Citrate (FC) on Serum Phosphorus Levels in ESRD Patients." This abstract has been selected by the ASN Program Committee for a Free Communication Session (oral presentation) during the ASN's Renal Week in San Diego, California. Date: Saturday, November 18, 2006 Session Name: Bone Disease in CKD Stage 5 Session Time: 4:00 PM - 6:00 PM Room: 4 Abstract Program Number: SA-FC029

Niecestro RM, et al. "Ferric Citrate (Phosphate Binder): Effects on Serum Iron and Other Parameters in ESRD Patients." This abstract will be published in the 2006 supplement of the Journal of the American Society of Nephrology (JASN).

Niecestro RM, Ferric Citrate for the Treatment of Hyperphosphatemia in ESRD. Abstract submitted to World Congress of Nephrology

Niecestro RM et al. A randomized double-blind, placebo-controlled, dose-ranging study on the effect of ferric citrate on serum phosphate in patients with end-stage renal disease. Manuscript in preparation

Diabetic Nephropathy

Raz I, Weiss, R, Niecestro R, McGill J, Knipnes M et al. Sulodexide for the treatment of diabetic nephropathy. Manuscript in preparation